Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/RU2004/000260	International filing date *(day/month/year)* 01.07.2004	Priority date *(day/month/year)* 14.07.2003

International Patent Classification (IPC) or national classification and IPC

A61K38/43, 38/46, A61P31/00, A61P3/10, 9/10

Applicant

GENKIN, Dmitry Dmitrievich

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of _____ sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/RU Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/RU2004/000260

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/RU2004/000260

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-4	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-4	NO
Industrial applicability (IA)	Claims	1-4	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The examiner's opinion has been established taking into account the applicant's reply submitted on 15.02.2005, and the following documents:

D1: US 6 391 607 B1

D2: US 6 033 846

D3: SERGEEVA L.M. Kliniko-laboratornaya otsenka mukoliticheskogo effekta pulmozima u bolnykh mukovistsidozom, PhD dissertation in medicine, Ekaterinburg, 1999

D4: GANNUSHKINA I.V. ET AL. Uroven DNK v plazme krovi bolnykh s aterosklerotycheskim porazheniem magistralnykh arterii golovy i bokovym amiotroficheskim sklerozom. Bulleten eksperimentalnoi biologii i medistiny, Meditsina, 1997, № 12, pages 610-612

D5: ZHONG S. ET AL., J. Clin. Pathol. 2000 Jun; 53(6): 466-9, abstract

D6: BURT M. ET AL., Liver Transpl. Surg., 1996 Sep; 2(5): 391-4, abstract

D1 discloses a method of treating infectious

diseases caused by bacteria, fungi or parasites, which includes a locally administered agent destroying extracellular DNA, namely a DNase enzyme.

Furthermore, administration of DNase into the blood circulatory system is known from D1, but for treatment of non-infectious diseases, accompanied by qualitative and quantitative change to blood extracellular DNA, in which blood extracellular DNA is part of immune complexes (IC). The examiner cannot agree with the applicant's arguments that D1 does not describe destruction of blood extracellular DNA as such, and relates only to destruction thereof as part of immune complexes, as the application point of DNase is by definition DNA. Therefore, although in D1 DNA is part of IC, it circulates in the blood and by definition is destroyed by DNase administered into the circulation. Furthermore, D1 shows the need to administer DNase in doses and regimes ensuring a high level of DNA-hydrolytic activity of blood plasma, controlling changes of blood extracellular DNA by gel electrophoresis.

D2 discloses the pathogenic role of blood extracellular DNA in case of different infections, including bacterial infections, and in case of somatic diseases, which consists in impairment of blood circulation, immune and coagulating system functions, and accretion of DNA in various organs.

D3 describes treatment of mucoviscidosis, a somatic disease caused by mutations of somatic gene cells and accompanied by qualitative and

quantitative change of extracellular DNA in phlegm, using administration of DNase, which destroys DNA when administered tracheobronchially. Furthermore, D3 shows the presence of changed blood extracellular DNA in case of mucoviscidosis.

D4-D6 respectively disclose qualitative and/or quantitative changes of blood extracellular DNA in case of atherosclerosis, sugar diabetes, and diseases connected with delayed type hypersensitivity reaction, in particular graft-versus-host reaction.

D1 is the prior art closest to the variant of the method for treating generalised infectious diseases specified in independent claim 1.

This variant differs from D1 in that in case of these diseases the agent destroying blood extracellular DNA is administered not locally but into the circulatory system. Therefore this method is novel.

However, such administration of this agent (DNase) for treatment of diseases accompanied by changes to blood extracellular DNA is known from D1, and the pathological role of blood extracellular DNA in case of the infections specified in the claim is known from D2.

Therefore, to a person skilled in the art it is obvious from D1-D2 to use an agent which destroys blood extracellular DNA (Dnase) by administration into the circulatory system for the treatment of said generalised infectious diseases, as changes of blood extracellular DNA being one of the

pathogenetic factors of the disease, which requires treatment accordingly.

Therefore, claims 1-2 in respect of treatment of generalised infections caused by bacteria, fungi or protozoa by means of DNase, an agent which destroys blood extracellular DNA when administered into the circulatory system, does not meet the requirement of inventive step.

As regards treatment of atherosclerosis, sugar diabetes, allergic diseases connected to delayed type hypersensitivity reaction, D4-D6 describe changes to blood extracellular DNA in case of these diseases. Therefore, taking into account the pathogenetic role of blood extracellular DNA in case of various somatic diseases known from D2, it is obvious for a person skilled in the art to act on this pathogenetic factor for the treatment of said diseases.

Therefore the method according to claim 1 in this respect also does not meet the requirement of inventive step.

As regards the variant of the method according to claim 1 for treating diseases resulting from mutation of somatic cell genes, as the pathogenetic role of blood extracellular DNA in such diseases, in particular in mucoviscidosis, is known from D2-D3, and systemic administration into circulation of an agent for destroying blood extracellular DNA is known from D1, in this respect claim 1 does not meet the requirement of inventive step.

The examiner cannot agree with the applicant's

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

view that D1 does not contain selection criteria of effective doses and regimes of administration of DNase "in vivo", as D1 shows that selection of specific doses and regimes of administering DNase depends on the type of disease, the characteristics of the patient, etc., and are selected in such a way as to support high hydrolytic activity of the blood in order to destroy a specific quantity of DNA, which is determined by gel electrophoresis. Therefore, a person skilled in the art can select said regimes and doses by empirical means, i.e. such a selection is obvious to a person skilled in the art. Therefore, claims 2-4 do not meet the requirement of inventive step.

Claims 1-4 meet the requirement of industrial applicability.